Aus dem Pathologischen Institut der Universität Düsseldorf
Direktor: Prof. Dr. med. W. Hort

CLASSIFICATION OF DYSPLASIAS IN COLORECTAL ADENOMAS

Qualitative and quantitative (karyometric) investigations.

DISSERTATION

zur Erlangung des Grades eines Doktors der Medizin

Der Medizinischen Fakultät der Universität Düsseldorf

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Introduction

With the increase of carcinomas of the large bowel the interest in carcinogenesis is now partly focussed to precancerous changes. Since the de-novo carcinogenesis in a flat mucosa occurs only seldom, if ever (12,24), most carcinomas probably develop from adenomas (20).

Several investigators have designated structural changes in adenomas as dysplasias; according to Riddell (27), dysplasia stands for changes "at a cytological level indicative of neoplastic transformation". According to this author the term atypia is less accurate meaning anything that is not typical, such as hyperplasia. Formerly, various attempts have already been made to describe precancerous changes in colorectal adenomas (30, 31, 6, 32).

Recently new classifications of dysplasia in large bowel adenomas have been proposed (22, 13, 20). Although cytoplasmic alterations occuring in the course of neoplastic transformation have been shown by histochemical techniques (4, 26) and electron microscopy (11, 21), however, first karyometric measurements have shown an enlargement of nuclei in adenomas and especially in carcinomas (28). At the same time the degree of dysplasia is dependent on structural changes of the neoplastic glands namely the degree of epithelial pseudostratification and tubular branching (13). The latter author distinguished 10 classes of premalignancy based on glandular branching and epithelial pseudostratification. A less sophisticated but more useful classification of dysplasia of Muto et al. (22) that was basic for the WHO-classification (19) also relies on structural changes within the mucosa more than on cellular pseudostratification. This study is concerned with the problem whether nuclear measures in addition to

structural alterations are reliable to classify dysplasias in adenomas of the large bowel.

Material and methods

Biopsies of 21 normal large bowel specimens and 36 adenocarcinomas of high and moderate differentiation and 141 large bowel adenomas were removed during endoscopy. 16 adenomas were excluded because of poor fixation or mechanical alterations. The adenomas were cut in slices of 2 to 3 mm, prepared in the Autotechnikon® and embedded in Paraplast®. Measurements were performed on sections which were about 3 µm thick. As a rule, these sections were stained by hematoxylin-eosin, exceptionally with the alcianblue-PAS stain, Gomori's silver impregnation and elastica van-Gieson stain.

Semiquantitative investigations:
In the residual 125 adenomas and 36 adenocarcinomas first the incidence of different structural patterns concerning nuclear form, pseudostratification, polarity, mucin content were listed semi-quantitatively. As certain structural characteristics turned out to correspond with alterations of nuclear morphology, the second part of this study was planned in order to make a detailed study of nuclear size by morphometry.

Karyometric studies:
Only areas with orthogradely cut glands were investigated. The longitudinal and transversal diameter of nuclei were measured by means of an eyepiece micrometer (ZEISS Company) of the size Kpl. 8x and the lens 95x in oil immersion. Usually, 40 to 50 adjacent nuclei were measured in a selected area. In areas of more complex growth, e.g. in bud-like or sieve-like structures, additional measurements were performed according to nuclear orientation within the glands, e.g. distinguishing nuclei at the base or at the crest of the buds and in the centre and periphery of the sieves. The mean values of the measurements from adenomas with identical structural patterns were comprised in groups. Repeated mesurements wihtin the same selected area showed only small variations which were below 10 % of the given value. Out of the given values of nuclear length and width, the area and the volume of nuclei in different groups of dysplasias were approximately calculated with the formulas of the ellipsoid area ($A = \pi ab$) and the volume of a rotation ellipsoid ($V = \frac{4}{3}\pi ab^2$), "a" being half of the maximal diameter and "b" half of the minimal diameter.

Measurements were performed in the middle and at the base of normal crypts, afterwards in twelve adenomas with different degrees of pseudostratification in order to see whether pseudostratification is related to different nuclear sizes and a relevant criterion of dysplasia. Then nuclear measurements were performed in selected areas of dysplasias in adenomas classified according to Muto et al. (22), and Morson and Sobin (19). Finally, the nuclear sizes were determined in 36 adenocarcinomas and 10 cases of transitional mucosa (8). Additional mesurements were performed in rare forms of dysplasia, e.g. solid dysplasia, mucinous and signetring cell dysplasia, which could not be grouped because of their low incidence rate.

Results

A. Qualitative and semiquantitative results

Mild dysplasias consist of basophilic rod epithelium with polar orientation of nuclei which show a palisading formation. The nuclei are elongated compared to the normal epithelium (fig. 1a, 3b). In 80 % of the investigated adenomas, there was palisading with 2 rows and in 20 % with 3 rows. Small mucine vacuoles existed in 77 % of the cases, but were not present in the residual 23 %.

Moderate dysplasias show intraepithelial budding and a slight loss of polarity of the nuclei (fig. 1b, 3c). At the base of the buds, the nuclei are more round and bleb-like, whereas at the crest of the buds they are elongated. Thus each bud resembles to a minute gland. Adjacent to these buds, there were, in 80 %, nuclei which are similar to those in mild dysplasia. 10 % of the investigated areas showed nuclei either with distinct differences of nuclear size or uniform bleb-like nuclei. Pseudostratification with 2 nuclear rows was found in 23 %, with 3 rows in 70 % and with 4 rows in 7 % (fig. 3d). The luminal row predominantly showed

mitotic figures. Many small secretory vacuoles were found in 17 %, and scattered mucin droplets in 67 %. Abnormal secretion in basal mucine vacuoles (fig. 3d) occured in 16 %. In 10 % of the cases only a narrow interstitial space was left between the glands with a tendency to dos-à-dos position.
Changes with merging of the crests of the buds and a focal transition into beginning sieve-like configurations were called "confluent buds". Tangential cutting may lead to a ropeladder-like appearance of the epithelia or to an arrangement of lumina looking like a string of pearls.

Severe dysplasias may consist of "tubulopapillar", cribriform, solid or mucinous and signetring cell dysplasias (fig. 2a-c).
In the most common pattern of cribriform growth, nuclear palisading is not only disturbed in the sieve-like structures, but also in the adjacent areas.
Only 10 % of the adjacent epithelium showed nuclear forms similar to mild dysplasia, whereas 90 % showed striking polymorphy. Within the centre of the sieve-like structures the nuclei sometimes were smaller, probably because of pyknotic changes. Sieve-like structures developed from pseudostratified areas with 1 or 2 nuclear rows in 15 %, from 2 or 3 nuclear rows in 71 %, and from glands with 4 and more nuclear rows in about 14 %. In all cases, only a few small secretory vacuoles were found, 81 % of which showed an abnormal position.
Severe "tubular or papillar" dysplasias showed a dos-à-dos position of glands in more than 60 %. Within the glandular lumina the epithelia form angular, sometimes pseudopapillary projections, thus giving the lumen a star-like or jaggy, dentated appearance. Cells may be extruded from the epithelial surface, and intraluminar debris may occur. These tubular or papillar severe dysplasias usually present large bleb-like nuclei

with prominent nucleoli.
Solid severe dysplasias were found in 2 large adenomas, once in the immediate environment of invasive carcinoma. These changes showed moderately large, fairly uniform oval nuclei and only few mitoses.
In all types of dysplasias there were groups of cells with abrupt cytoplasmic eosinophilia. However, they appeared more often in higher degrees of dysplasia.

Among the invasive adenocarcinomas of high or moderate differentiation (fig. 3e, f) the nuclei were situated in 1 or 2 rows in 39 %. In 61 % there was a pseudostratification with 2 or 3 rows. The polar orientation of nuclei was disturbed or entirely abolished in all cases. In 75 % the nuclei were bleb-like and slightly anisomorph, whereas in 25 % there also was an abrupt change from bleb-like to hyperchromatic elements. Besides drop-like deformity or further polymorphy nuclear enfoldings were found. Isolated mucine vacuoles usually showed an abnormal position within the cytoplasma.
According to the classification of the WHO, tubulopapillar carcinomas were listed as highly differentiated and cribriform carcinomas as moderately differentiated. Additional qualitative stromal features of these carcinomas, like desmoplasia, immunocytic, histiocytic, and leucocytic invasion of large bowel cancers (3) were not evaluated in this study.

B. Karyometric results

Normal colo-rectal mucosa.

The mean nuclear dimensions (maximal vs. minimal diameter) in the region of the crypt base were 6.8 $\pm$ 0.4 vs. 3.8 $\pm$ 0.4 μm, and in the middle region 7.3 $\pm$ 0.6 vs. 2.5 $\pm$ 0.3 μm. The nuclear area in the base of the crypts

was 20.3 μm^2 and in the middle of the crypts 14.6 μm^2. The nuclear volumes may thus be calculated as 51.9 μm^3 at the base of the crypts and 24.6 μm^3 at the middle of the crypts.

Adenomas with various degrees of pseudostratification (Kozuka's criteria).

The mean nuclear dimension (max vs. min. diameter) which were measured in 12 adenomas were 12.7 ± 1.6 vs. 3.8 ± 0.7 µm in epithelia with one nuclear row, 13.9 ± 2.0 vs. 4.3 ± 0.6 µm in epithelia with 2 rows, and 13.4 ± 1.1 vs. 3.6 ± 0.4 µm in epithelia with 3 and more nuclear rows. There is no significant correlation between the nuclear dimensions and the degree of pseudostratification.

Adenomas with dysplasias defined by Muto et al. (22) and Morson and Sobin (19).

In mild dysplasia there was an elongation of nuclear length from 7.3 µm (normal mucosa, middle region of the crypts) to 12.8 ± 1.4 µm, corresponding to an increase of 74.5 %. The mean values of the nuclear width increased from 2.5 µm to 3.4 ± 0.3 µm, corresponding to an increase of 34 % (fig. 4). Thus the calculated nuclear areas are doubled, and nuclear volumes are increased three fold compared with normal epithelium in the middle of the crypt (fig. 4, 5; table 1).

In moderate dysplasia nuclear dimensions varied according to the measurements being made either on the crest or on the base of the buds or in the adjacent areas. In the adjacent areas there were nearly the same values for nuclear length and width as in mild dysplasia. The figures amounted to 12.8 µm length vs. 3.3 µm width, the nuclear area to 32.8 μm^2, and the nuclear volume to 71.0 μm^3. On the crest of the buds the nuclear dimensions were 15.0 ± 1.0 vs. 2.9 ± 0.4 µm, the calculated nuclear

area 34.3 μm^2 and the nuclear volume 66.6 μm^3. At the base of the buds the nuclei showed a medium length of 9.7 ± 1.5 μm and an average width of 4.9 ± 0.7 μm, the calculated nuclear area summed to 31.8 μm^2 and the nuclear volume to 88.7 μm^3 (see table 1).
The medium values for moderate dysplasia (combinated from crest and base of the buds) were calculated as 12.3 μm for the nuclear length vs. 3.5 μm for the nuclear width, 33.8 μm^2 for the nuclear area and 78.9 μm^3 for the nuclear volume.
Striking results were found in the sub-group of "confluent buds": The nuclear length of 12.9 ± 4.8 μm being comparable to the values in mild dysplasia, the nuclear width, however, amounted to 5.7 ± 0.9 μm. Thus the average nuclear area comes up to 57.7 μm^2 and the nuclear volume to the 9-fold.

In severe dysplasia mainly cribriform glands were measured, the periphery of which structures showed nuclear dimensions of 16.8 ± 2.3 vs. 5.8 ± 1.1 μm corresponding to a nuclear area of 77.0 μm^2 and a nuclear volume of 299.8 μm^3. The centres of the sieves showed nuclear dimensions of 10.2 ± 1.0 vs. 6.4 ± 1.5 μm, the calculated nuclear area in the centres was 51.5 μm^2 and the nuclear volume 221.1 μm^3.
Compared to the nuclear size in the middle of the crypts of normal colo-rectal mucosa, there is a striking increase of nuclear size in the periphery of the sieves - both lengths and widths of the nuclei are enlarged to 129 or 130 % (fig. 4).

In 6 cases of severe "tubulopapillar" dysplasia the nuclear data were 19.4 ± 1.3 vs. 6.1 ± 0.8 μm (max. vs. min. diameter), the calculated area was 92.2 μm^2 and the nuclear volume 372.5 μm^3. Among the severe "tubulopapillar" dysplasias one case of marked cytoplasmic eosinophilia showed a medium nuclear length of 18.6 μm and a nuclear width of 8.2 μm.

In 1 case of solid dysplasia the average nuclear size was 12.8 vs. 6.1 µm.

Adenocarcinomas.

Because of nuclear polymorphy there was a scattering of measurements in the single case and in the whole group of carcinoma.
The mean nuclear sizes of 6 highly differentiated tubular or papillary adenocarcinomas differed only slightly: The average nuclear length was 19.8 ± 1.5 µm, the average width 7.2 ± 0.3 µm, these data summing up to a nuclear area of 106.7 μm^2 and a volume of 509.2 μm^3.
In the sieve-like structures of the 30 moderately differentiated carcinomas the values for the max. and min. nuclear diameter were 18.9 ± 1.8 µm vs. 6.9 ± 1.4 µm. The nuclear area was 100.7 μm^2 and the nuclear volume 454.3 μm^3. The last value means an increase to the 20-fold of the nuclear volume as compared to the normal epithelium in the middle of the crypts.

Transitional mucosa.

In this group there was a medium nuclear length of 10.2 ± 0.8 µm and a medium width of 3.3 ± 0.4 µm. The calculated area of these nuclei was 26.4 μm^2, the calculated nuclear volume was 58.2 μm^3. These data show that the transitional mucosa has to be arranged just into the gap between normal epithelium and mild dysplasia.

Discussion

Although nuclear morphology plays an important rôle in the identification of malignant tumours, there is a striking lack of karyometric data.
To our knowledge Oehlert et al. (23) were the first to apply karyometrical studies in gastric mucosa in order to characterize different degrees of dysplasias when describing different forms of gastric d ysplasia.
According to our investigations, nuclear changes, besides alterations of the glandular structure, represent an important diagnostic criterion of colo-rectal dysplasia.

The method of measuring nuclear dimensions cannot be employed without reservation, however. One condition for such karyometric measurements is the orthograde section of nuclei parallel to their longitudinal axes. Because of complex winding of the neoplastic glands only focal measurements within the sections are possible. The results may be influenced by bioptic procedures and variations in the bioptic technique and by slight alterations during processing of the tissues. Furthermore when measuring the nuclei in 760-fold magnification, one unit of the eyepiece micrometer corresponds roughly to one micrometer; therefore, the widths of normal and mildly dysplastic nuclei being about 2.5 - 4 µm could not always be measured with absolute precision. This limitation of the method, however, does not apply to the enlarged bleb-like nuclear structures in higher digrees of dysplasia. Finally, the polymorphous nuclei in carcinomas can only roughly be described by the morphometric parameters. In spite of these objections, nuclear dimensions in severe epithelial dysplasia and carcinoma surmount those in normal crypts and low grade dysplasias so much that the dimensions of a possible methodological error may be neglected. Furthermore, repeated control measurements show the reliability of such karyometric measurements.

Our karyometric results of the normal mucosa show that the nuclei of the goblet cell epithelium have mean diameters of 7.3 vs. 2.5 µm in the middle of the crypts The nuclei in the proliferative compartment at the base of the crypts are somewhat shorter and broader.
As for the colo-rectal adenomas, in mild dysplasia the

the nuclear lenghts increaseby 74 %, and the nuclear widths by 34 %, the calculated nuclear area thus increases by 135 %, and the volume by 210 % (fig. 4, 5). In moderate dysplasia with intraluminal budding the size of nuclei differs at the crest and the base of the buds. The values of nuclear area are within the same range as those of mild dysplasia. Because of the differences of nuclear forms and cellular arrangement the buds in moderate dysplasia are suggestive of crypts en miniature and we believe that they represent newly established compartments of cellular proliferation. It may be conceived that bud formation is related to a disproportionately quick growth of epithelial cells in comparison to stromal septa;thus a bigger area for tumour cells being provided by pseudopapillar budding on the same stromal surface.

The changes that we called "confluent buds" according to our nuclear measurements represent an intermediate group between moderate and high degrees of dysplasia. With a nuclear length similar to mild dysplasia and more than a doubled nuclear width the calculated nuclear area in these confluent buds is increased to the 4-fold, and the nuclear volume to the 9-fold of normal values.

In severe dysplasia, especially papillary structures show an even more pronounced elongation and broadening of nuclei which are comparable to tubulopapillary adenocarcinomas. In sieve-like dysplasias there are similar broad, bleb-like nuclei, whereas the nuclear length is less increased. The centres of these cribriform areas show reduced nuclear dimensions which might be consistent either with regressive changes because of poor nutrition and pressure atrophy or with a twisting of the nuclei from the plane of section.

Finally, in the adenocarcinomas there is a remarkable increase of the nuclear size. There are comparable results in tubulopapillary and in sieve-like adenocarcino-

mas, the mean lengths of which are increased by 3 times and the widths by 2.6 times as compared to normal crypt epithelium. The nuclear volume is increased to the 18.5-fold of the control value. The problem of different nuclear morphology in invasive adenocarcinomas with various degrees of differentiation (1) cannot be discussed within the scope of this study.

Although the pseudostratification of epithelia was considered to be one main criterion of dysplasia by Kozuka (13), according to our results this is not significantly related to alterations in nuclear morphology. Since other cytological and structural alterations (fig. 6) seem to be more important, Kozuka's graduation into five groups and two further groups distinguished by different degrees of tubular branching ist not helpful both under a practical viewpoint and according to our morphometric studies. The pseudostratification of epithelium in large bowel adenomas seems to indicate a high cell turnover and thus, in a limited way, a criterion of dedifferentiation. As only some of the higher differentiated carcinomas show pseudostratification and many other carcinomas widely lack this feature, this morphological criterion is not decisive for distinction of carcinomas or adenomas.

The different forms of dysplasia and carcinoma show different mean values of nuclear length and width. However, the distribution curves (fig. 4) show some overlap of the nuclear dimensions, and some of the carcinomas even have relatively short nuclei down to 15.7 µm. Large nuclei usually show other features like prominent nucleoles or enfoldings of the nuclear membrane (5). Besides the different nuclear dimensions, this simple criterion may offer an additional help in distinguishing low and moderate degrees of dysplasia and carcinoma.

Rare forms of dysplasia have recently been described in ulcerative colitis (14, 27): e.g. adenomatous dysplasia, basal cell proliferation, pancellular dysplasia and in-situ anaplasia. Moreover, Otto and Gebbers (25) also found epidermoid metaplasia. We have not seen these special forms of dysplasia in the course of the investigations of colo-rectal adenomas and carcinomas. The solid dysplasias described by us seem to occur very seldom, as we could find them only twice among several hundreds of adenomas. Although nuclear dimensions revealed relatively small nuclei, we are inclined to classify solid dysplasias as severe dysplasia, first because of a beginning invasive adenocarcinoma in the immediate proximity in one case, second because of a structural loss. We would not accept these as epidermoid metaplasia, since we could not demonstrate keratins in the lesion by the immunoperoxidase method (unpublished result). This example shows that severe alterations of glandular structure on one hand and lower nuclear size on the other hand may appear independently in rare cases. Such a dissociation between structural and nuclear atypias, according to our results, is relatively rare; if it occurs in solid and cribriform structures, the dysplasias should be classified as severe (table 2).

The differentiation between moderate and tubulopapillar dysplasias and even carcinomas may be difficult unless nuclear size and additional qualitative diagnostic criterias are applied. The former has not been reported in the available literature. The neoplastic tubulopapillar glands with severe dysplasia consist of notched, dentated lumina with accumulation of cellular debris and dos-à-dos position of adjacent glands (fig. 6).

In the differential diagnosis between adenoma and in-

vasive carcinoma besides invasion across the muscularis mucosae Fisher and Turnbull (9) and Helwig (10) have pointed out the importance of the desmoid stroma reaction.

In the investigated adenomas there are different populations of dysplasias, which can be traced histotopically (2); they correspond to different stemlines within one tumour (16, 17).

The nuclear enlargement shown in this study is obviously the consequence of a polyploidisation of genetic material which has been proven by cytophotometry (29, 15, 7, 18, 16). Additionally, nuclear enlargement may be due to functional metabolism, e.g. accumulation of histones. According to these studies, early adenomatous changes show a normal diploid karyotype (18) whereas there are extensive alterations with hyperdiploid or -triploid values in adenocarcinomas (29). Enterline and Arvan (7) also found hyperploidy in adenomas with villous parts. In these studies, poorly differentiated adenocarcinomas showed less polyploidy than the highly differentiated ones, however. Because of these profound differences in DNA content in various adenomas and carcinomas or even within the same adenoma, the nuclear DNA content is not an absolute criterion for the distinction between colo-rectal adenomas and carcinomas.

In conclusion our findings suggest that dysplasias in colo-rectal adenomas can be conveniently graded by the classification of Muto et al. (22); our morphometrical data confirm this classification although it has not been defined precisely until now. We propose a complex extension of this classification which comprises several cytological and structural parameters. The single data are depicted in fig. 6 and listed in table 2. Although the individual criteria may be contro-

versial, according to our observations usually the structural and nuclear atypies coincide thus giving a fairly reproducable diagnostic spectrum which is of help in difficult cases.

Summary

In this qualitative and quantitative study, 125 adenomas, 36 adenocarcinomas, 21 normal mucosas, and 10 transitional mucosas were investigated. The different criteria for dysplasia given by Kozuka (13) and Morson and Sobin (19) were examined under a karyological aspect. In areas with certain structural patterns like pseudostratification, intraepithelial buds, formation of sieve-like or solid structures, nuclear lenghts and widths were determined.

The normal rectal mucosa shows nuclear dimensions (length vs. width) of 7.3 vs. 2.5 µm. The basophilic rod epithelium has an average nuclear length of 12.8 µm and a width of 3.4 µm. On the other hand, severe dysplasias of various histologic structures show a nuclear length of 18.1 µm and a width of 6.1 µm (average of the various groups). Such severe epithelial dysplasias and high or moderately differentiated adenocarcinomas show identical morphometric measurements. Between low and high grade dysplasia, there is an intermediate group with the formation of intraepithelial buds which seem to represent newly established proliferation compartments. The nuclear dimensions of this group are partly similar to mild dysplasia, partly, especially if confluent buds are found, similar to severe epithelial dysplasia. Apart from this, solid, signetring-cell and mucinous dysplasias as well as eosinophilic cytoplasmic alterations have been described. The various forms of dysplasia occur together within the adenomas. The nuclear alterations are interpreted as an expression of polyploidisation and chromosomal aberration. In difficult cases the simple nuclear measurements may contribute to the differential diagnosis between light and severe dysplasias or carcinoma in biopsies.

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Legends to the figures:

Fig. 1: Common forms of dysplasia in colorectal adenomas.

a): Mild dysplasia with straight tubules containing a basophilic rod epithelium with 3 rows of nuclei (HE, x80).

b): Moderate dysplasia with irregular glandular budding and a rod epithelium with up to five nuclear rows. There is inverted mucous secretion (HE, x70).

c): Severe dysplasia with cribriform glandular structure and loss of nuclear polaritiy (HE, x70).

Fig. 2: Uncommon forms of dysplasia in colorectal adenomas.

a): Solid dysplasia (HE, x70).

b): Mucinous dysplasia (HE, x70).

c): Signet ring cell dysplasia (HE, x120).

Fig. 3: Nuclear size and arrangement in various forms of dysplasia.

a): Normal goblet cells with one row of small nuclei.

b): Mild dysplasia with enlarged nuclei arranged in 2-3 rows.

c): Moderate dysplasia with glandular bud; nuclei at the base of the bud are round whereas the nuclei at the crest of the bud are slender.

d): Moderate dysplasia with nuclear crowding and up to 5 nuclear rows. Inverted mucous secretion.

e): Invasive carcinoma with bleb-like, large nuclei, multiple prominent nucleoli and dark squeezed cells.

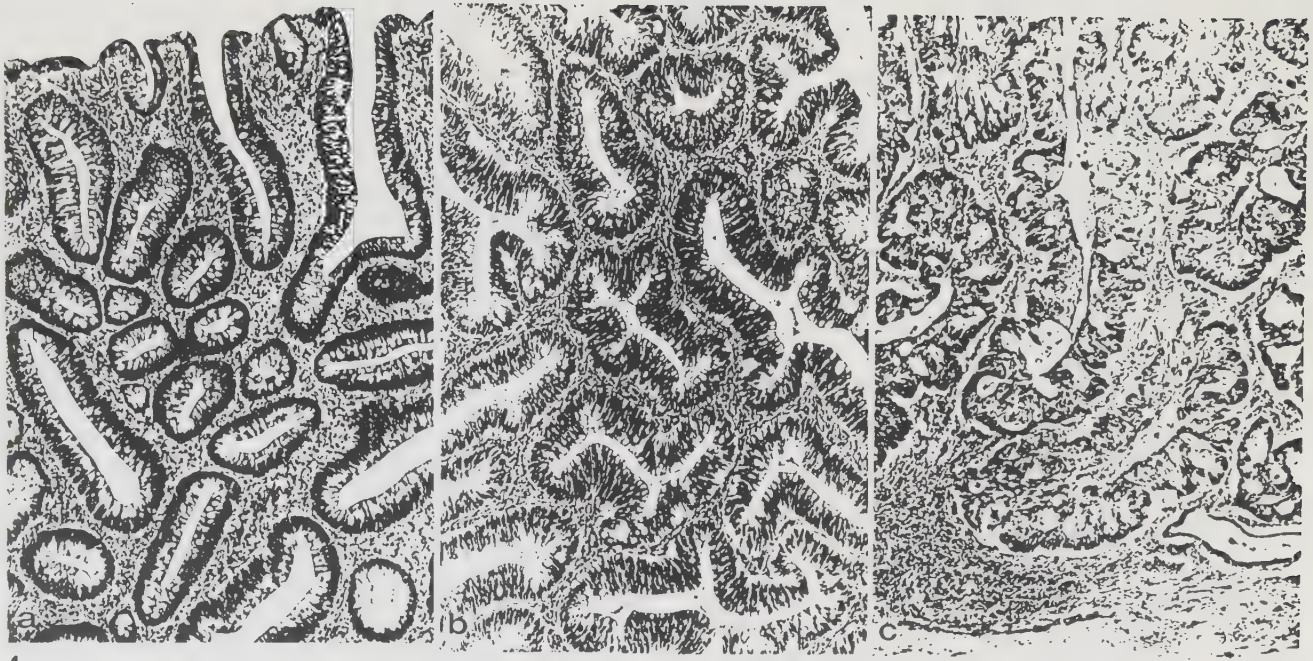
f): Severe dysplasia with similar nuclear morphology like e).

All sections HE and x1000, except for d) (x750).

Fig. 4: Column diagrams of nuclear width and length in colorectal adenomas and carcinomas.

Fig. 5: Nuclear areas and volumes in various neoplastic lesions of the large bowel.

Fig. 6: Structural and cytological characteristics of various forms of dysplasia and of carcinomas.



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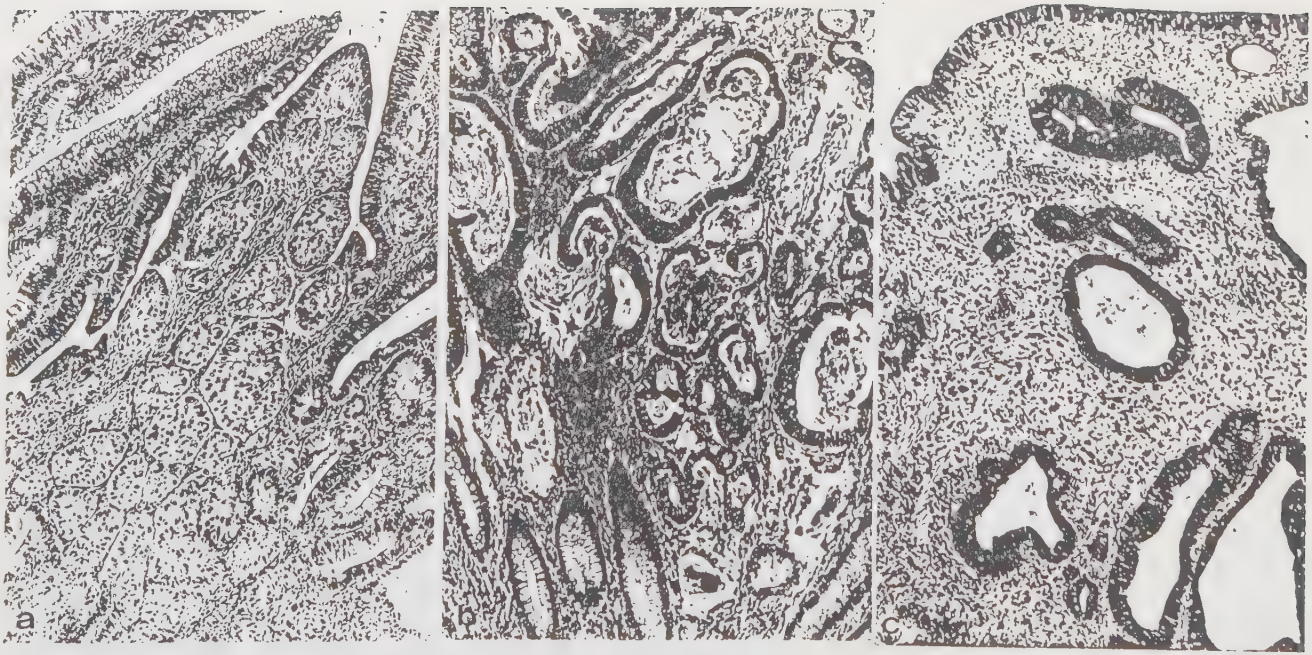

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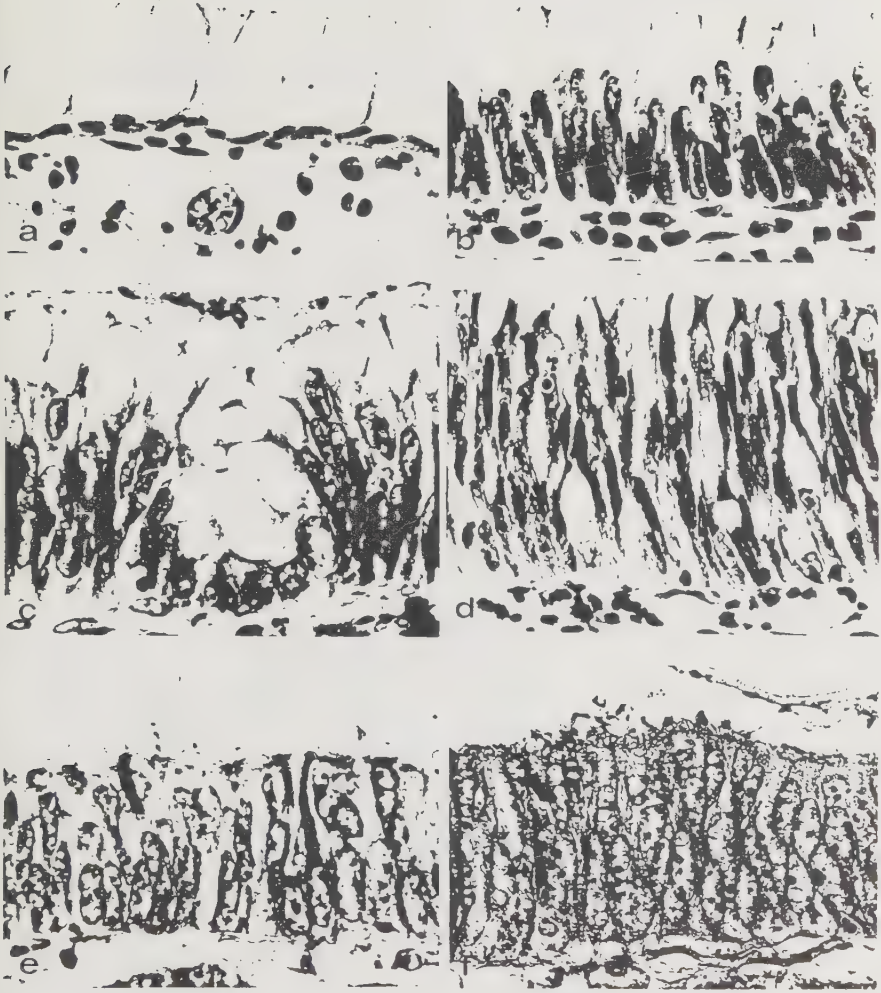
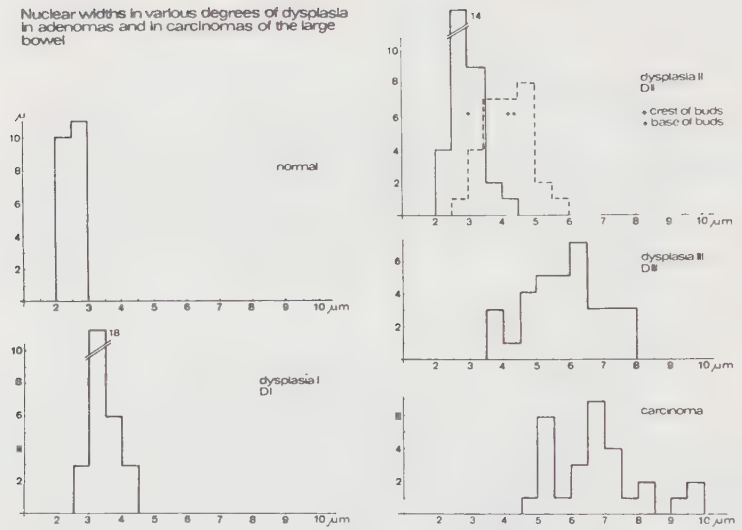
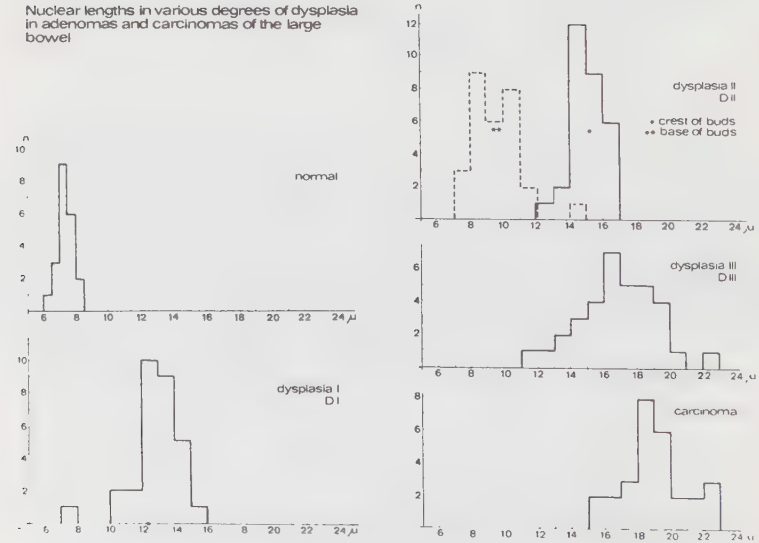


3

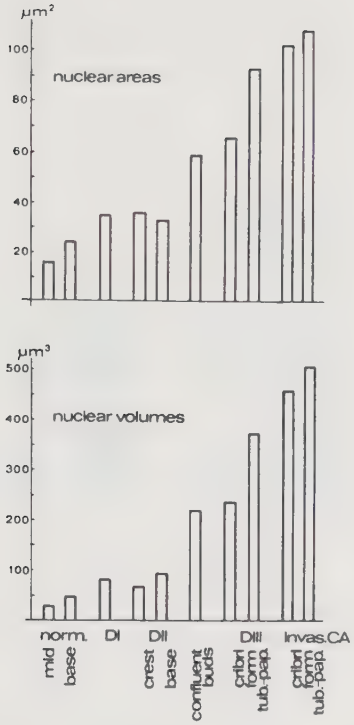
Nuclear widths in various degrees of dysplasia in adenomas and in carcinomas of the large bowel



Nuclear lengths in various degrees of dysplasia in adenomas and carcinomas of the large bowel



4a,b



Calculated areas and volumes of cell nuclei in various neoplastic lesions of the large bowel

structures :
tubulo - papillar
cribriform
solid
diffuse
dysplasia I
dysplasia II
dysplasia III
invasive carcinoma

	(n)	LENGTH (μm)	WIDTH (μm)	AREA (μm^2)	VOLUME (μm^3)
NORMAL MUCOSA (MIDDLE OF CRYPT)	21	7,3 ± 0,6	2,5 ± 0,3	14,6	24,6
(BASE OF CRYPT)	11	6,8 ± 0,4	3,8 ± 0,4	20,3	51,9
TRANSITIONAL MUCOSA	10	10,2 ± 0,8	3,3 ± 0,4	26,4	58,2
MILD DYSPLASIA	30	12,8 ± 1,4	3,4 ± 0,3	34,1	76,9
MODERATE DYSPLASIA (CREST OF BUD)	30	15,0 ± 1,0	2,9 ± 0,4	34,3	66,6
(BASE OF BUD)	30	9,7 ± 1,5	4,9 ± 0,7	31,8	88,7
"CONFLUENT BUDS"	14	12,9 ± 4,8	5,7 ± 0,9	57,7	219,4
SEVERE DYSPLASIA "TUBULOPAPILLAR"	6	19,4 ± 1,3	6,1 ± 0,8	92,2	372,5
CRIBRIFORM					
(PERIPHERY)	34	16,8 ± 2,3	5,8 ± 1,1	77,0	299,8
(CENTRE)	10	10,2 ± 1,0	6,4 ± 1,5	51,5	221,1
INVASIVE ADENOCARCINOMA					
TUBULOPAPILLAR	6	19,8 ± 1,5	7,2 ± 0,3	106,7	509,2
CRIBRIFORM	30	18,9 ± 1,8	6,9 ± 1,4	100,7	454,3

AVERAGE NUCLEAR MEASUREMENTS IN NEOPLASTIC COLORECTAL LESIONS

TABLE 1

DYSPLASIA	HISTOLOGICAL FEATURES				CYTOLOGICAL FEATURES					
	EPITHELIAL STRUCTURE	NUCLEAR ROWS	POLARITY	LUMEN	STROMAL AREA	NUCLEAR LENGTH	NUCLEAR WIDTH	NUCLEOLUS	MITOSIS	CYTOPL.
MILD	TUBULAR TUBULOVILLOUS VILLOUS	1-3(4,5)	+++	ROUND	+(+)	13	3	(+)	+	BAS.
MODERATE	BUD-EPITHELIUM	3-6	+(-)	BUDDING	+	15	3	+	++	BAS./ EOS.
	CONFLUENT BUDS	3-6	+/-	(SIEVE)	+/-	13	6	++	++	EOS.
SEVERE	TUBULOPAPILLAR	1-2(-6)	±/-	DENTATED	+/-	19	6	+++	++(+)	EOS.
	CRIBRIFORM	1-2(-3)	-	SIEVE-LIKE	+/-	13	6	++(+)	++(+)	EOS.
	SOLID			NO	+/-	12	6	++	++	EOS.
INVASIVE CARCINOMA	TUBULAR-PAPILLAR	1-2(-4)	±/-	DENTATED	DESMOPLASIA	18	7	+++	+++	EOS.
	CRIBRIFORM			SIEVE-LIKE						

TABLE 2

Lebenslauf

Geb. am 11.5.1955 in Neheim-Hüsten, Kreis Arnsberg, Nordrhein-Westfalen. Erstes Kind von Paul Schwermann und Agnes Schwermann, geb. Renner.

Schulbildung: Volksschule Veitshöchheim/Würzburg 1962-1966; Riemenschneider-Gymnasium in Würzburg (Neusprachlicher Zweig) 1966-1975. Abitur Juni 1975.

Studium der Humanmedizin: Univ. Würzburg 1975-1977, Univ. Düsseldorf 1977-1980, Univ. Erlangen 1980-1982.

Staatsexamen und Approbation als Arzt: Mai 1982.

Berufliche Tätigkeit: Juli 1982 bis August 1983 als Assistenzarzt im Pathologischen Institut der Stadt Nürnberg (Leitung: Prof. Dr. Pließ). Seit August 1983 als Assistenzarzt in der Medizinischen Klinik des Caritaskrankenhauses Bad Mergentheim (Leitung: Prof. Dr. Bundschu).

Eheschließung mit Susanne Schwermann, geb. Hirner im April 1983.

Herrn Prof Dr. Borchard möchte ich meinen besonderen Dank aussprechen: Er hat mich unermüdlich mit Rat und Tat unterstützt.

Druckerei A. Staudenraus Würzburg